REMARKS

In the Claims:

The Examiner has indicated that claims 25-29, 32-34, and 38-41 are allowed.

Claim 35 has been amended to clarify that the claimed isolated nucleic acid which hybridizes, under high stringency conditions, to SEQ ID NO: 1 or to the nucleic acid encoding the polypeptide of SEQ ID NO:2 also has the property of encoding a polypeptide that stimulates release of proteoglycans from cartilage tissue. No new matter is added by this amendment, and it is supported at pages 137-138 of the specification.

Claim 36 has been amended to clarify that the claimed high stringency conditions comprise 50% formamide, 5 x SSC (0.75 M sodium chloride, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5 x Denhardt's solution, sonicated salmon sperm DNA (50 µg/ml), 0.1% sodium dodecyl sulphate, and 10% dextran sulfate at 42°C, with washes at 42°C in 0.2 x SSC (0.75 M sodium chloride, 0.075 M sodium citrate) and 50% formamide at 55°C, followed by a high-stringency wash consisting of 0.1 x SSC (0.75 M sodium chloride, 0.075 N sodium citrate) containing EDTA at 55°C. No new matter is added by the amendment, and it is supported at page 30, lines 17-21.

Claim 42 has been amended to clarify that the claimed nucleic acid has 0-20 conservative amino acid substitutions. No new matter is added by this amendment, and it is supported at page 61 of the specification.

Claim 43 is cancelled herein without prejudice or disclaimer.

Rejections Withdrawn:

Applicants thank the Examiner for withdrawing the rejection of claims 25-29, 32-34, and 38-41 under 35 U.S.C. § 112, first paragraph for scope of enablement; for withdrawing

rejection of claims 25-29, 32-34, and 38-41 under 35 U.S.C. § 112, first paragraph for written description; for withdrawing rejection of claims 25-27, 36, and 38-41 under 35 U.S.C. § 112, second paragraph for indefiniteness; for withdrawing rejection of claim 37 under 35 U.S.C. § 102(b) as being anticipated by Dreher *et al;* and for withdrawing the objection to claims 28, 29, and 32-34.

Request for Reconsideration:

Claim Rejections under 35 U.S.C. § 112, first paragraph:
Enablement:

The Examiner has maintained rejection of claims 35-37 under 35 U.S.C. § 112, first paragraph, alleging that one skilled in the art would be forced into undue experimentation to practice the invention as broadly as it is claimed. Specifically the Examiner contends that the claims are remarkably broad and encompass a genus of nucleic acids that vary substantially both in length and in nucleotide composition. As an example, the Examiner argues that the specification fails to teach an artisan how to use the variants of the nucleic acid encoding SEQ ID NO:2 that do no possess the same activity as that of the nucleic acid encoding the amino acid of SEQ ID NO:2.

Applicants have amended claim 35 such that any claimed nucleic acid that hybridizes to SEQ ID NO:1 or to the nucleic acid encoding the polypeptide of SEQ ID NO:2 must encode a polypeptide that stimulates release of proteoglycans from cartilage tissue. Thus, one of skill in the art would know how to use variants of SEQ ID NO:2 that hybridize under high stringency conditions. Applicants have overcome this ground of rejection and respectfully request that it be withdrawn.

The Examiner rejected claim 42 for overbreadth, noting that the claim scope encompasses a sequence where every amino acid of SEQ ID NO:2 is substituted. The Examiner kindly noted that an acceptable percent amino acid/or nucleic acid sequence identity is required to overcome the rejection of claim 42. Per the Examiner's kind

suggestion, claim 42 has been amended to encompass a sequence with only 0-20 conservative amino acid substitutions. SEQ ID NO: 2 is 379 amino acids long. Thus, an amino acid sequence with 20 conservative amino acid substitutions would have 94.7% sequence identity to SEQ ID NO:2. This is an acceptable percent amino acid/nucleic acid sequence identity and therefore, Applicants have overcome this ground of rejection and respectfully request that it be withdrawn.

Written Description:

The Examiner has maintained rejection of claims 35-37 under 35 U.S.C. § 112, first paragraph for lack of written description. The Examiner contends that the claims encompass "an enormous genus of nucleic acids that vary substantially both in length and in nucleotide composition." Specifically, the Examiner argues that the claims do not require that the nucleic acid possesses any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature."
Applicants have amended claim 35 to clarify that the claimed isolated nucleic acid which hybridizes, under high stringency conditions, to SEQ ID NO: 1 or to the nucleic acid encoding the polypeptide of SEQ ID NO:2 also has the property of encoding a polypeptide that stimulates release of proteoglycans from cartilage tissue. Thus, the amended claims require that the hybridizing nucleic acid not only hybridize under high stringency conditions and encode a polypeptide that stimulate release of proteoglycans, but also allow one of skill in the art to distinguish nucleic acids within the scope of the claimed genus from those falling outside the scope of the claimed genus.

The Examiner further argues that the specification fails to provide a reasonable number of representative species of the claimed genus. Applicants respectfully disagree.

The analysis for determining whether the present specification provides written description support for the invention defined by claims 35-37 may be performed by numerous methods, several of which are described in the Guidelines and further exemplified in the Revised Interim Written Description Guidelines Training Materials ("Written Description Training Materials"), published on the USPTO website at

http://www.uspto.gov/web/offices/pac/writtendesc.pdf. These Written Description Training Materials provide additional clarity to the Guidelines published in the Federal Register, Volume 66, No. 4, pages 1099-1111.

With regard to claims 35-37, the present situation is analogous to Example 9 found at pages 35-37 of the Written Description Training Materials. More specifically, in Example 9 on pages 35-37 of the enclosed Written Description Training Materials, a claim directed to "[a]n isolated nucleic acid that specifically hybridizes under highly stringent conditions to the complement of the sequence set forth in SEQ ID NO:1, wherein said nucleic acid encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity" is analyzed for compliance with the written description requirement. In this example, the essential feature of the claimed invention is the isolated nucleic acid that hybridizes to SEQ ID NO:1 under highly stringent conditions and encodes a protein with a specific function. There is a single species disclosed (a molecule consisting of SEQ ID NO:1) that is within the scope of the claimed genus. Finally, the art indicates that hybridization techniques using a known DNA as a probe under highly stringent conditions was conventional in the art at the time of filing. The Written Description Training Materials conclude that the above claim is supported by an adequate written description because "a person of ordinary skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs." The Written Description Training Materials also conclude that disclosure of a single cDNA sequence in this context is a sufficient representative number of species.

All of the just-mentioned requirements are met by this application as well as the currently pending claims. In particular, the essential feature of amended Claims 35-37 is an isolated nucleic acid that hybridizes to SEQ ID NO:1 or to the nucleic acid encoding the polypeptide of SEQ ID NO:2, and which also has the property of encoding a polypeptide that stimulates release of proteoglycans from cartilage tissue. There is a species (SEQ ID NO:1) disclosed within the scope of the claims and high stringency

conditions were both well known in the art as of the filing date of the present application and are defined at page 30 of the specification.

Given the abovementioned factors, Applicants respectfully submit that Claims 35-37 satisfy the written description requirement of 35 U.S.C. § 112, first paragraph, and therefore, respectfully request that this ground of rejection be withdrawn.

The Examiner also rejects claim 42 under 35 U.S.C. § 112, first paragraph for lack of written description alleging that due to the breadth of the claimed genus and the lack of the definitive structural features of the genus, one skilled in the art would not recognize from the disclosure that Applicants were in possession of the claimed genus.

Applicants respectfully disagree. Applicants have amended claim 42 to encompass a sequence with only 0-20 conservative amino acid substitutions. As discussed above, SEQ ID NO: 2 is 379 amino acids long and therefore, an amino acid sequence with 20 conservative amino acid substitutions would have 94.7% sequence identity to SEQ ID NO:2. Thus, amended claim 42 is not overly broad. Further, one of ordinary skill in the art would recognize from the required functional identity and sequence identity that Applicants had possession of this claimed genus at the time of filing. Hence, Applicants have overcome this ground of rejection and respectfully request that it be withdrawn.

New Matter:

Applicants have cancelled claim 43 herein without prejudice or disclaimer and therefore respectfully request that this ground of rejection be withdrawn.

Claim Rejections Under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 35 and 37 as being indefinite. The Examiner alleges that claim 35 is indefinite because it recites "under high stringency conditions," without defining the hybridization conditions in the claims. The Examiner contends that neither the art, nor the specification, provides an unambiguous definition of what qualifies as "high stringency conditions."

Applicants respectfully disagree. At page 30, lines 12-21 of the specification, Applicants specifically define "high stringency conditions" as:

> . . . those that: (1) employ low iconic strength and high temperature for washing, for example 0.015M sodium chloride / 0.0015 M sodium citrate/0.1% sodium dodecyl sulfate at 50°C; (2) employ during hybridization a denaturing agent, such as formamide, for example, 50% (v/v) formamide with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50mM sodium phosphate buffer at pH 6.5 with 750 mM sodium chloride, 75 mM sodium citrate at 42°C; or (3) employ 50% formamide, 5 x SSC (0.75 M NaCl, 0.075 M sodium citrate, 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5 x Denhardt's solution, sonicated salmon sperm DNA (50 µg/ml, 0.1% SDS, and 10% dextran sulfate at 42 °C, with washes at 42 °C in 0.2 x SSC (sodium chloride/sodium citrate) and 50% formamide at 55 °C, followed by a high-stringency wash consisting of 0.1 x SSC containing EDTA at 55 °C.

Applicants note that they have previously directed the Examiner's attention to the above definition found on page 30 of the specification. In response, the Examiner argued that the definition only provides exemplary conditions and pointed to the use of "for example" on page 30.

Applicants respectfully disagree. The definition of "high stringency" found on page 30 of the specification from line 12-21 only uses the phrase "for example" to refer to one example of a denaturing agent that might be used. Other than that example, the definition of "high stringency conditions" found on page 30 is not exemplary and use of the phrase "as defined herein," indicates that Applicants intended to set forth a definition of "high stringency conditions."

Further, Applicants disclose that additional detail and explanation of stringency of hybridization reaction may be found at Ausubel et al., *Current Protocols in Molecular Biology,* Wiley Interscience Publishers (1995). Thus "high stringency conditions" as used in claims 35 and 37 is not indefinite.

Applicants have overcome this ground of rejection and respectfully request that the Examiner reconsider and withdrawn this rejection of claims 35 and 37.

Claim Rejections Under 35 U.S.C. § 102(b):

The Examiner has maintained rejection of claims 35 and 36 under 35 U.S.C. § 102(b) as being anticipated by Dreher *et al.* Applicants have amended claim 35 to clarify that the claimed isolated nucleic acid which hybridizes, under high stringency conditions, to SEQ ID NO: 1 or to the nucleic acid encoding the polypeptide of SEQ ID NO:2 also has the property of encoding a polypeptide that stimulates release of proteoglycans from cartilage tissue. Dreher *et al.* does not teach that the disclosed nucleic acid sequence encodes a polypeptide that stimulates release of proteoglycans from cartilage tissue. Hence, claims 35 and 36 are not anticipated by Dreher *et al.,* because according to the MPEP § 2131, "a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Thus, Applicants have overcome this ground of rejection and respectfully request that it be withdrawn.

Conclusion

The Examiner has allowed claims 25-29, 32-34, and 38-41. Applicants believe that currently pending Claims 35-37 and 42 are also allowable. Hence, Applicants respectfully request that the Examiner grant allowance of this application. The Examiner is invited to contact the undersigned attorney for Applicants via telephone if such communication would expedite the prosecution this application.

Respectfully submitted,

C. Noel Kaman

C. Noel Kaman
Registration No. 51,857
Attorney for Applicant

BRINKS HOFER GILSON & LIONE
P.O. BOX 10395
CHICAGO, ILLINOIS 60610
(312) 321-4200